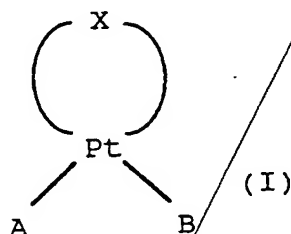


CLAIMS

1. A method for labeling nucleotides comprising the steps of:

- reacting a reactive moiety of a linker of the formula



wherein X represents any stabilizing bridge and wherein A and B represent the same or different reactive moieties, with an electron donating moiety of a spacer, which spacer comprises a chain having at least four atoms and at least one heteroatom in the chain, which spacer further comprises said electron donating moiety at one end of the chain and a reactive moiety at the other end of the chain;

- reacting the reactive moiety of said spacer with a label;
- reacting the other reactive moiety of said linker with a nucleotide.

2. A method according to claim 1 wherein the label is biotin, avidin, streptavidin, digoxigenin or a functional equivalent thereof.

3. A method according to claim 1 or 2 wherein the nucleotide is adenine, thymidine, cytosine, guanine or uridine or a derivative thereof.

4. A method according to any of the preceding claims wherein the electron donating moiety is an amine or a thiolate anion.

5. A method according to claim 4 wherein the amine is an aromatic amine.

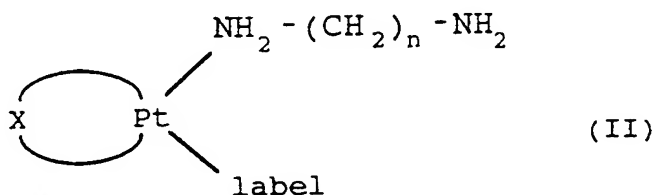
6. A method according to any of the preceding claims wherein at least one heteroatom is an oxygen atom.

5 7. A method according to any of the preceding claims wherein the spacer comprises no more than 20 carbon atoms in the chain and wherein the chain is essentially non-branched.

10 8. A method according to claim 7 wherein the spacer is 1,8-diamino-3,6-dioxaoctane.

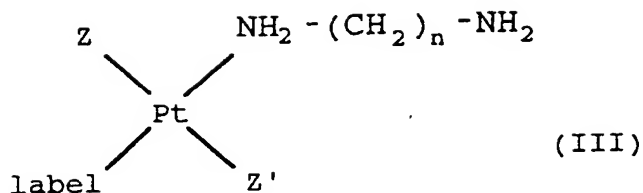
9. A method according to claim 7 wherein the spacer is an oligolysine or a polylysine.

15 10. A method according to claims 1-4 wherein the linker is reacted with a labeling moiety comprising a label and a spacer, which labeling moiety has the formula



20 or the formula

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wherein X represents any stabilizing bridge, Z and Z' represent a non-leaving ligand and n is an integer of from 2 to 10.

11. A method according to claim 10, wherein Z and/or Z' represent an NH_3 , NH_2R , NHR_2 , or NR_3 group, wherein R represents an alkyl group having from 1 to 6 carbon atoms.

12. A method according to any of the preceding claims, wherein X represents an aliphatic diamine.

13. A method according to claim 12 wherein X represents an aliphatic diamine having 2-6 carbon atoms.

14. A method according to claim 13 wherein X is an ethylene diamine group.

15. A method according to claims 12-14 wherein one or both of the nitrogen atoms of the aliphatic diamine are shielded.

16. A method according to claim 15 wherein one or both of the nitrogen atoms of the aliphatic diamine are substituted with an alkyl group of from 1 to 6 carbon atoms.

17. A method according to claim 16 wherein one or both of the nitrogen atoms of the aliphatic diamine are substituted with one or two methyl groups.

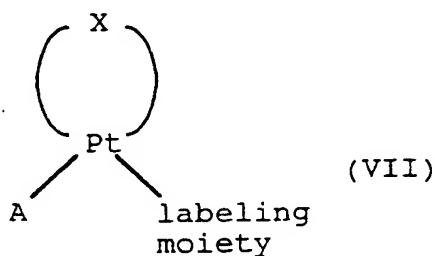
5 18. A method according to any of the preceding claims wherein A and/or B are selected from the group consisting of NO_3^- , SO_3^- , Cl^- , I^- , or other halogens.

10 19. A method according to any of the preceding claims wherein A and B are the same.

20. A labeled nucleotide obtainable by a method according to any of the preceding claims.

15 21. A labeled nucleotide according to claim 20 wherein the spacer is an oligolysine or a polylysine.

22. A labeling substance having the formula



20 wherein X represents any stabilizing bridge, A represents a reactive moiety and the labeling moiety comprises a label and a spacer, which spacer comprises a chain having at least four
25 atoms and at least one heteroatom in the chain, which spacer further comprises an electron donating moiety at the end of the spacer distal from the label.

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